

Applicants: Dean Engelhardt *et al.*

Serial No.: 08/486,066

Filed: June 7, 1995

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recitation appears, *inter alia*, in dependent claims 239, 273 and 309 (now canceled) and in original claim 1 (now canceled). Claims 238, 272 and 308 are further amended to include the recitation that "Sig is a moiety which is detectable when said nucleotide is incorporated into a double-stranded nuclei acid duplex." Support for this claim language appears throughout the specification, and therefore it is respectfully submitted that no new matter has been added by the present amendment.

Claims 239, 273 and 309 are canceled as their recitation is now in amended independent claims 238, 272 and 308.

All of the pending claims (except 239, 273 and 309, now canceled) stand rejected under 35 U.S.C. § 112, first paragraph, as being nonenabled by the specification. It is said that the specification is enabling only as to attachment of the Sig or PM moieties to the 2', 3' and 5' positions of ribose or deoxyribose sugars.

Though Applicants do not agree with the Examiner, to advance this application to issuance, all three of the independent claims 238, 272 and 308 are amended as above noted to recite that the Sig and PM moieties are attached to the 2', 3' or 5' positions of a ribose or deoxyribose sugar.

Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. § 112 is traversed and should be withdrawn.

All of the claims, except claims 244, 247, 248, 250-54, 257-61, 263, 278, 281, 282, 284-88, 291-95, 300, 314, 318, 320-24, 327, 328, 334 and 335, stand rejected under 35 U.S.C. §

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102(a) as being anticipated by Caruthers and/or under 35 U.S.C. § 102(b) as being anticipated by Kourilsky.

Caruthers is said to disclose deoxyribose nucleotides having detectable Sig moieties such as dimethoxy-trityl or acetyl as well as a phosphate moiety attached to SM in the form of a phosphine. Kourilsky is said to disclose the preparation of nucleotides, deoxynucleotides, and oligomers thereof, having biotin, mercury and SH group labels. The polynucleotides are said to attach to a particular nucleotide via sugar-phosphodiester backbone with linked Sig and phosphate moieties attached.

In view of the above amendments and the following remarks, these rejections are respectfully traversed.

Caruthers discloses a method for chemically synthesizing deoxyoligonucleotides comprising detritylation of a deoxynucleoside linked to a silica gel support, condensing thereon a tritylated deoxynucleoside, blocking unreacted nucleoside hydroxyl groups, and oxidation of the phosphite to the phosphate. This method is repeated sequentially until a deoxyoligonucleotide of the desired length and composition is synthesized. The synthesized deoxyoligonucleotide is then stripped from the silica support and purified.

In Caruthers, tritylated deoxynucleotides are employed only as a means to form an oligomer chain. In each synthesis sequence, the trityl moiety is stripped off and replaced with a new nucleotide. The completed deoxyoligonucleoside once stripped from the support and purified is not tritylated.

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Caruthers does not disclose a nucleotide having moiety covalently attached to a sugar which is detectable when the nucleotide incorporated into a double-stranded nucleic acid duplex as is required by the present amended claims. The trityl moieties of the nucleotides of Caruthers are removed in the synthesis of the deoxyoligonucleosides. There are no trityl moieties detectable should the deoxyoligonucleosides of Caruthers be incorporated int a double-stranded nucleic acid duplex.

Further, Caruthers provides no suggest to alter its disclosed method to somehow arrive at Applicants' claimed invention. It is essential to the synthesis method of Caruthers that the trityl moieties be removed to build the oligomer.

And, even if the trityl moieties could be left on the oligomer, there is no disclosure in Caruthers that such would in any way be beneficial, let alone be detectable in a double-stranded nucleic acid duplex.

Accordingly, it is respectfully submitted that Caruthers neither discloses, suggests or otherwise renders unpatentable Applicants' invention as presently claimed.

Kourilsky discloses a method for detecting and characterizing a nucleic acid sequence in a specimen. The detecting probes are modified by attachment of a chemical or group or label (e.g., biotin) capable of complexing with an enzyme (e.g., B-galactosidase). To add biotin to the probe, Kourilsky teaches use of the so-called Manning technique. No other labeling technique is disclosed or suggested in Kourilsky, other than an unspecified "known" method of modification with metallic ions.

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In the Manning technique, the biotin does not bind to the sugar moiety of nucleotide. Instead, in the Manning technique formaldehyde crosslinks the nucleotide base with amines on cytochrome c and the biotin is thus bridged by the cytochrome c to the nucleotide base.

Therefore, Kourilsky does not disclose Applicants' claimed invention.

Further, Kourilsky provides no suggestion to modify the Manning technique in any way, let alone in a manner that might bind a detectable moiety to a sugar moiety.

Accordingly, it is respectfully submitted that Kourilsky neither discloses, suggests or otherwise renders unpatentable Applicants' claimed invention.

As neither Caruthers nor Kourilsky disclose or suggest the presently claimed invention, and as no secondary references have been applied, it is respectfully requested that the amendments be entered, the rejections be reconsidered and withdrawn, and the claims be allowed and passed to prompt issuance.

Alternatively, it is respectfully requested that the amendments be entered as placing the claims in better form for possible appeal.

If a telephone conference would further the prosecution of the application, Applicants' undersigned attorney requests that he be contacted at the telephone number below provided.

A fee of \$110.00 for a one-month extension of time is due in connection with this Amendment and authorization is given to charge this fee to Deposit Account no. 05-1135. In any

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other fee is deemed necessary in connection with this Amendment, authorization is hereby given to charge the amount of such fee to Deposit Account No. 05-1135.

Respectfully,

John J. Santalone / GM

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